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RADIOACTIVE MICROSPHERE STUDY OF CEREBRAL BLOOD FLOW UNDER ACCE--ETC(U)
NOV 80 K J GREENLEES, J E YODER, D M TOTH
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NOVEMBER 1980

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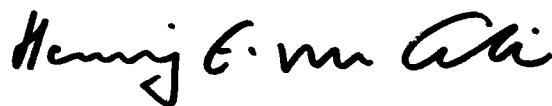
TECHNICAL REVIEW AND APPROVAL

The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals, "Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER



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Biodynamics and Bioengineering Division
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PREFACE

The research presented here was conducted by personnel of the Air Force Aerospace Medical Research Laboratory, Aerospace Medical Division, Air Force Systems Command, Wright-Patterson Air Force Base, Ohio, under work unit 72221050, "Brain Blood Flow." This research was supported in part by the Laboratory Director's Fund.

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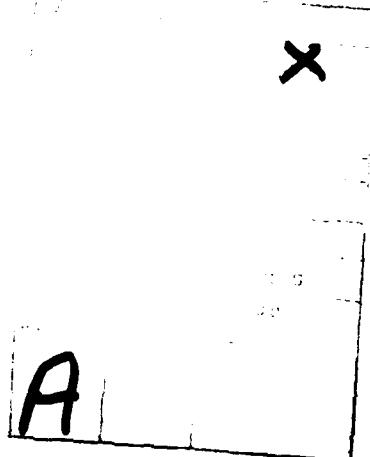


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INTRODUCTION

The Air Force Aerospace Medical Research Laboratory (AFAMRL) is involved in a major effort to design a predictive model of human operator performance under conditions of physiologic and psychologic stress. The effect of positive G_z acceleration on cerebral blood flow is a critical factor in predicting operator response. Howard and Glaister (1964) reported distinctly separate perfusion response characteristics for white and grey matter in man under acceleration stress, based on Xenon-133 clearance technique. They suggested a preservation of grey matter blood flow at the expense of white matter at $3G_z$. The use of radiolabelled microspheres to measure organ blood flow was first described by Rudolf and Heyman (1967). Since that time there have been many attempts to improve this method for use in total and intraorgan flow measurements. The purpose of this study was to quantify the effects of $3G_z$ and $5G_z$ acceleration on regional cerebral blood flow in the unprotected baboon (*Papio-papio*). This information could then be added to the data base used in predicting human operator performance.

METHODS

Eleven baboons were used in this study. Their weight, sex, and level of G_z exposure are presented in Table 1. These animals had previously been exposed to a similar acceleration profile for cardiac output determinations using the thermal dilution technique (Yoder et al., 1978; Yoder et al., 1979). All animals were housed in the AFAMRL Veterinary Sciences Division vivarium and fasted 16 hours before each experiment. On the day of the experiment the baboon was anesthetized with Ketamine® and transported to the medical analysis laboratory for surgical preparation. The use of Ketamine® was continued to assure proper anesthesia during surgery. A polyethylene catheter (PE210) was threaded through the left femoral artery and placed so that the tip was in the left ventricle. Position was determined by a characteristic ventricular pressure trace. This catheter was used for injection of the microsphere suspensions. A second catheter was advanced in the right femoral artery so that the tip was in the proximal descending aorta for reference sample withdrawal. Position was again determined by the pressure tracing. Typically, the catheter was advanced into the ventricle and then backed off 2 cm. The animal was then placed in an Oloff Primate Restraint System (patent 412066) and moved to the animal platform of the Dynamic Environment Simulator. This multiaxis centrifuge was under the control of a predetermined computer program to ensure a reproducible acceleration profile.

A system for the sequential injection of up to five separately labelled radioactive microsphere suspensions was developed by an AFAMRL effort. This system has a federal patent pending. It is described in detail by Greenlees et al. (1980). This system was loaded with 15 micron radioactive tracer microspheres (3M Company) in a 0.05% solution of Tween-80. Five cartridges were prepared containing microsphere suspensions with Iodine 125, Cerium 141, Chromium 51, Strontium 85, and Scandium 46.

Following recovery from anesthesia, a Harvard withdrawal pump was activated to begin reference blood sample withdrawal at 15.3 mg/min. Fifteen seconds later a baseline Iodine 125 microsphere suspension was injected. The reference sample

TABLE 1
SUBJECT DESCRIPTION

Designation	Sex	Weight lb	G _z
A33	F	17.5	3
A35	F	18.5	3
E92	M	17.0	3
E96	M	19.0	3
F28	M	24.0	5
F30	M	21.0	5
F34	M	24.0	5
F36	M	25.0	5
F38	M	27.0	5
F40	M	24.5	5
F42	M	21.0	5

withdrawal was stopped after a total of 45 seconds. A new syringe was placed in the Harvard pump, and reference sampling was resumed. This was followed in 15 seconds by the beginning of acceleration. Cerium 141 microspheres were injected at target G_z (either 3G_z or 5G_z). This was followed by the injection of Chromium 51, Strontium 85 and Scandium 46 at 30-second intervals. Thirty seconds after the final microsphere injection, the centrifuge was brought to rest. Total time at positive G_z was 120 seconds. This profile is illustrated in Figure 1.

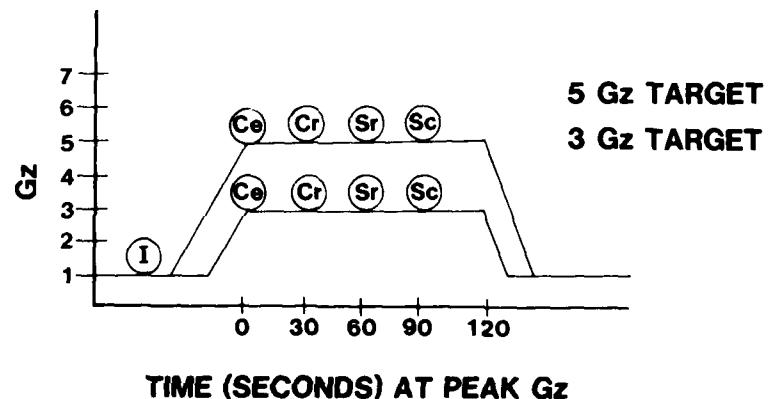


FIGURE 1 MICROSPHERE INJECTION PROFILES

The animal was killed with Euthanol® and an immediate necropsy was performed. The entire brain was removed, weighed, and placed in a formalin solution for 48 hours to facilitate dissection. The brain was then reweighed and sagitally bisected. The entire right half was weighed, sliced and placed into a series of preweighed vials for gamma counting. These vials were treated as a single sample to obtain an entire half brain average. The left half was dissected into easily identified anatomical groups, identified in Table 2.

TABLE 2
SAMPLE IDENTIFICATION

50	Superior occipital gyrus	58	Pons
51	Inferior parietal lobe	59	Medulla
52	Superior temporal gyrus	60	Copra quadrigemine
53	Middle and Inferior temporal gyrus	61	Corpus callosum
54	Superior temporal and post central gyri	62	Thalamus
55	Precentral gyrus	63	Hypothalamus
56	Cingulate gyrus	64	Internal capsule
57	Frontal lobe	65	Cerebellum

Each of the individual groups was placed in a separate preweighed counting vial. Blunt dissection, using scalpel handle and fingers, removed each of the cerebral gyri (superior occipital, inferior-parietal, superior-temporal, and cingulate). These were sliced and placed into individual preweighed counting vials. The entire cerebellum was removed and sliced to fill a preweighed vial. The remaining brain core was placed on a cutting board and the medial surface was removed in a 1.0 to 1.5 cm thick slice using a brain knife. The remaining core was sliced and placed in a counting vial. Several straight line cuts were made with a scalpel dissecting this medial slice to remove the pons, copra quadrigemina, thalamus, medulla, and corpus callosum. A separate, preweighed counting vial was used for each of these samples. The remaining brainstem was identified as hypothalamus and placed in a single preweighed vial. The tissue samples were counted in a Packard Auto-Gamma Spectrometer®. A computer program was developed to calculate tissue blood flow and cardiac output. This program, based on the method of Rudolf and Heyman (1967) was published by Smith et al. (1979).

RESULTS

Cardiac output measurements at $3G_z$ and $5G_z$ are reported in Table 3. Tissue flows, calculated in ml/min/g, are reported in Table 4 for the $3G_z$ and Table 5 for $5G_z$.

TABLE 3
CARDIAC OUTPUT
L/min

	Baseline	Peak G	G + 30 sec.	G + 60 sec.	G + 90 sec.
$3G_z$	A33	1.06	1.21	1.14	4.46
	A35	3.37	0.85	0.91	0.76
	E92	10.9	1.91	1.75	1.63
	E96	6.17	1.70	1.40	1.40
	F28	3.90	1.63	1.95	1.20
$5G_z$	F30	1.90	0.52	0.58	0.38
	F34	1.28	1.01	2.89	5.39
	F36	1.29	1.67	0.75	0.27
	F38	2.46	2.01	8.54	3.22
	F40	1.44	0.32	0.59	0.27
	F42	0.44	0.14	0.16	0.05
					0.07

TABLE 4
TISSUE FLOW FOR ANIMALS EXPOSED TO 3G_z
ml/min/g (Median Values)

Sample No	Baseline	Peak G	G + 30 sec.	G + 60 sec.	G + 90 sec.
50	1.00	0.62	0.52	0.57	0.76
51	0.99	0.59	0.51	0.48	0.90
52	1.14	0.72	0.58	0.60	1.00
53	0.99	0.51	0.67	0.45	0.78
54	1.13	0.59	0.54	0.44	0.51
55	1.02	0.55	0.49	0.42	0.70
56	0.86	0.61	0.46	0.59	0.53
57	0.87	0.33	0.46	0.45	0.31
58	2.55	1.14	0.88	1.03	0.73
59	1.04	0.39	0.45	0.07	0.83
60	2.06	0.85	0.81	1.01	1.36
61	0.55	0.36	0.23	0.26	0.33
62	1.86	0.80	0.69	0.91	0.98
63	1.34	0.41	0.50	0.70	0.88
64	0.91	0.45	0.46	0.49	0.73
65	1.14	0.42	0.57	0.66	0.67

TABLE 5
TISSUE FLOW FOR ANIMALS EXPOSED TO 5G_z
ml/min/g (Median Values)

Sample No	Baseline	Peak G	G + 30 sec	G + 60 sec.	G + 90 sec.
50	0.80	0.47	0.19	0.09	0.07
51	0.65	0.31	0.15	0.07	.09
52	1.03	0.44	0.18	0.08	0.10
53	0.71	0.49	0.19	.09	.007
54	0.67	0.25	0.12	0.06	0.06
55	0.66	0.33	0.12	0.04	0.07
56	0.85	0.34	0.13	0.08	0.09
57	0.78	0.33	0.21	0.10	0.12
58	0.69	0.40	0.30	0.16	0.25
59	0.83	0.46	0.40	0.21	0.21
60	1.39	0.66	0.53	0.19	0.12
61	0.38	0.19	0.07	0.03	0.03
62	1.22	0.61	0.35	0.16	0.15
63	0.88	0.42	0.23	0.13	0.24
64	0.71	0.37	0.16	0.06	0.09
65	0.78	0.53	0.38	0.20	0.14

Nonparametric statistical analysis was used to handle the data in view of the wide variability. A confidence interval of 87.5% was found for the 3G_z group and 96.9% for the 5G_z group. Cerebral samples were grouped and statistically analysed in the sections illustrated in Table 6. Results are reported as percent change from baseline or as the percentage of the cardiac output per 100 gm of tissue. Figures 2 and 3 show the percent change in blood flow as a function of time at 3 and 5G_z respectively. Figures 4 and 5 show flow as percent of cardiac output per 100 g of tissue using the same areas and conditions for 3G_z and 5G_z, respectively. A confidence interval for the half brain average flow is included in each of the graphs.

TABLE 6
CEREBRAL SECTIONS

Section	Sample No.
Occipital lobe	50
Parietal lobe	51, 54
Temporal lobe	52, 53
Frontal lobe	55, 56, 57
Brainstem	58 - 64
Cerebellum	65

The blood flow determination shows clearly that there is no single major area of the brain that appears to be preserved at the expense of the surrounding tissues. The reduction in flow at $3G_z$ was not significantly different from baseline in any of the areas listed in Table 3. All areas were significantly decreased from baseline after 90 seconds of $5G_z$ exposure. Analysis of the data in terms of percent cardiac output per 100 g of tissue again does not identify any area that is significantly preserved or sacrificed when compared to the half brain average.

DISCUSSION

The information gathered thus far has not demonstrated any region within the brain that is either especially vulnerable or resistant to the effects of acceleration on blood flow. Much of this can be attributed to the extreme variability of the data collected. A major factor influencing this is the variability of the cardiac output measurements. This has been shown to be typical of acceleration stress (Yoder et al., 1978). In addition, pooling of blood in the lower abdomen and extremities accentuates any propensity to arrhythmia by decreasing venous return (Ernsting, 1965). Placement of the injection catheter within the ventricle is another irritant factor.

Minor changes in regional blood flow could well have been masked during this study. Any factor that might reduce the data variability could improve the resolution to a degree that these minor changes would be identified. This would permit more effective use of the tremendous volume of data already produced by this study. A statistical reevaluation of the experimental results has been initiated. This analysis will be used as a factor in the consideration of future studies and the application of the results of this one. We hope that this will determine whether some of the variability seen in our data was physiologic or a result of the microsphere technique.

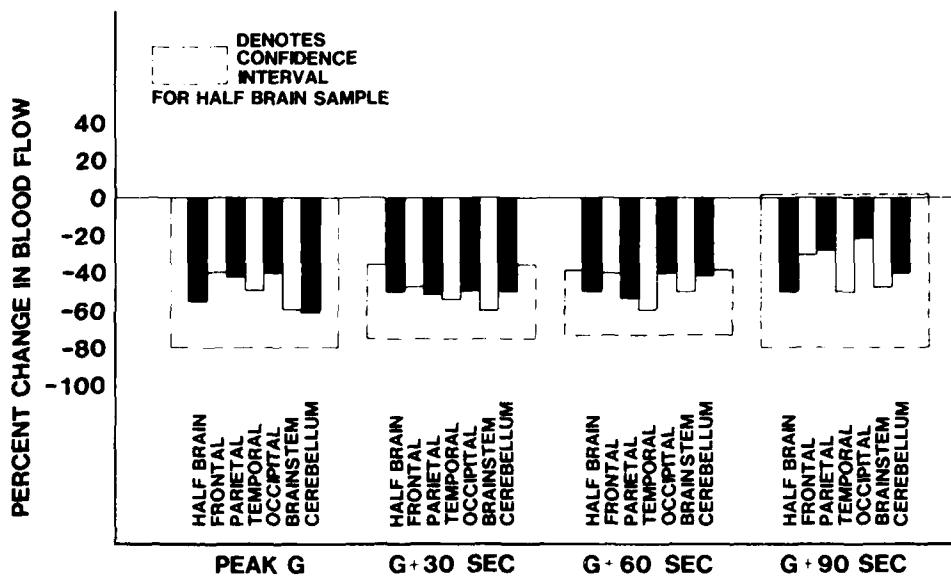


FIGURE 2 PERCENT CHANGE IN BLOOD FLOW AS A FUNCTION OF TIME AT $3G_z$ (MEDIAN VALUES)

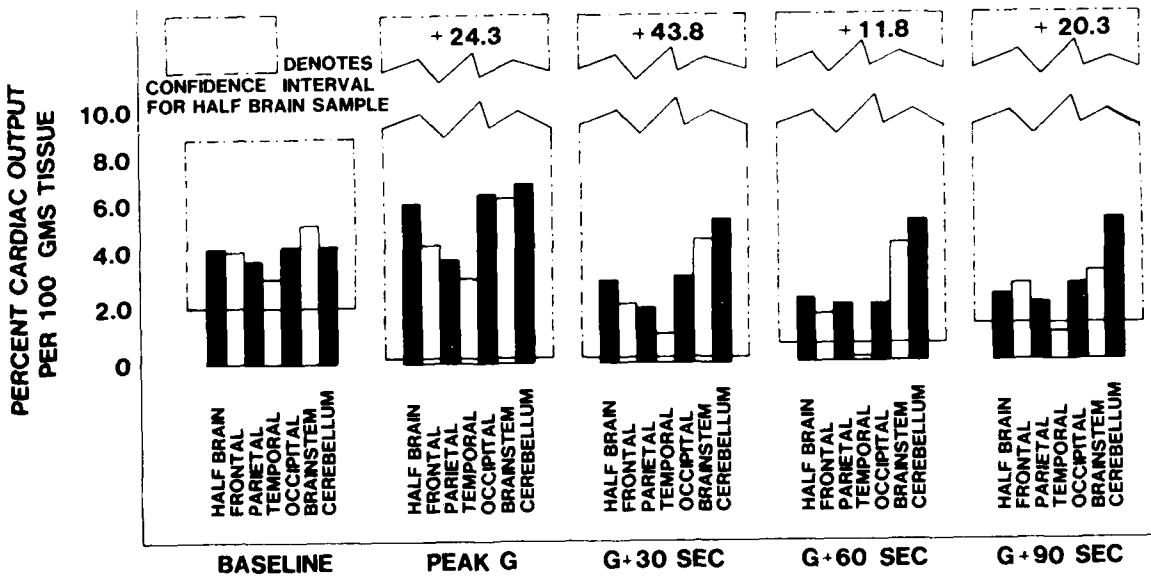


FIGURE 3 PERCENT CARDIAC OUTPUT PER 100 G TISSUE AS A FUNCTION OF TIME AT $5G_z$ (MEDIAN VALUES)

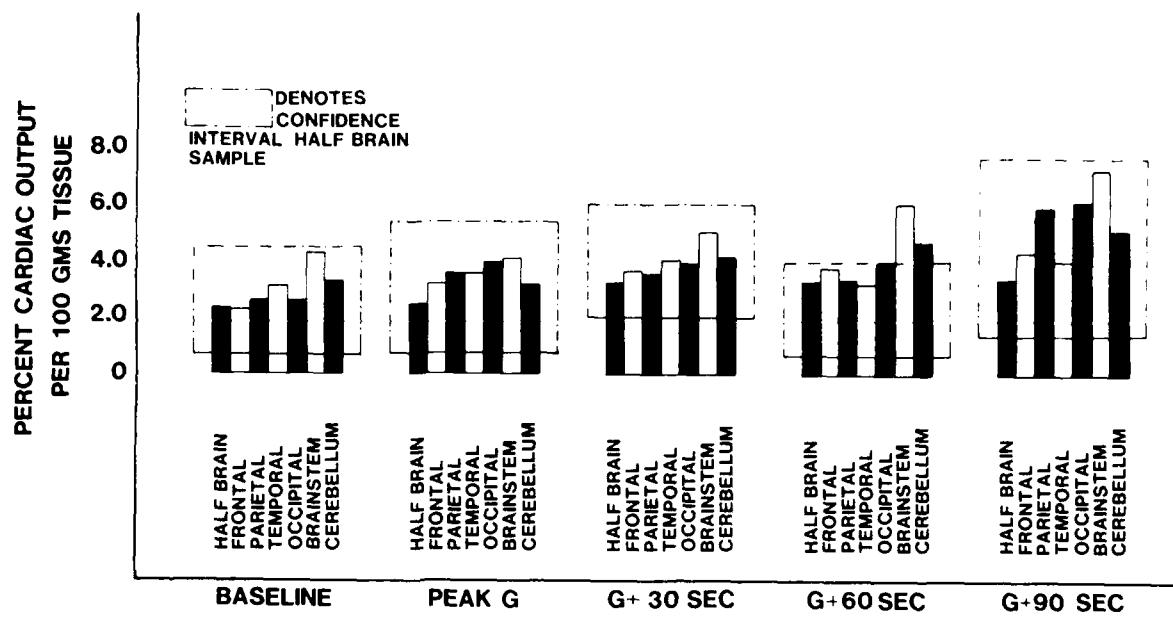


FIGURE 4 PERCENT CARDIAC OUTPUT PER 100 G TISSUE AS A FUNCTION OF TIME AT $3G_z$ (MEDIAN VALUES)

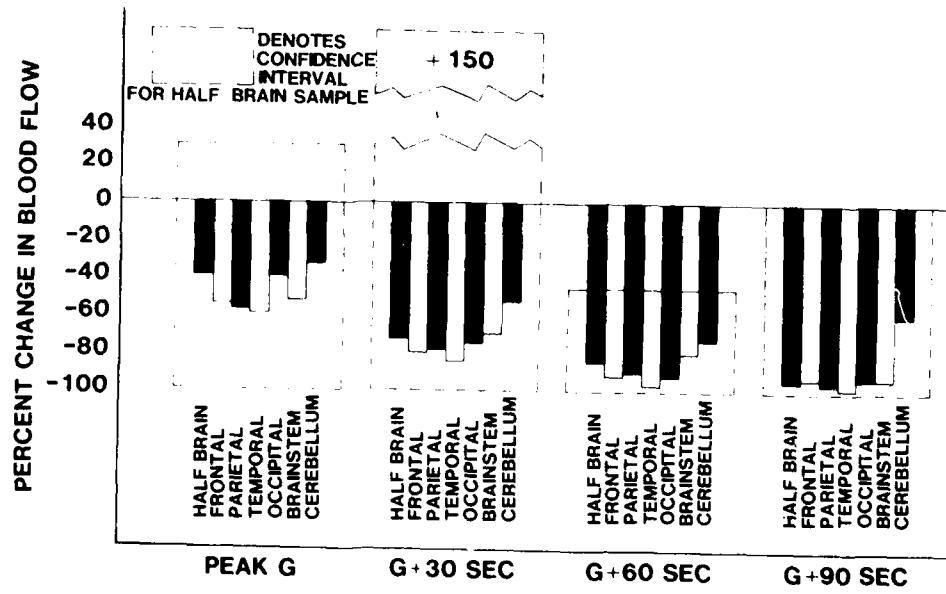


FIGURE 5 PERCENT CHANGE IN BLOOD FLOW AS A FUNCTION OF TIME AT $5G_z$ (MEDIAN VALUES)

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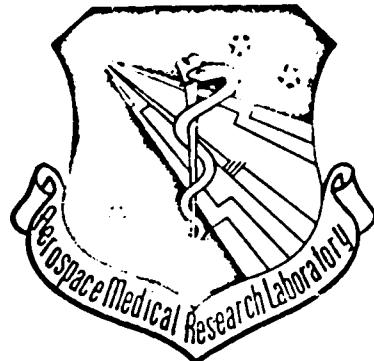
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